Rejection of Claims 12, 13, 23-26 and 30 Under 35 USC § 103.

Applicants have amended claim 12 (on which claims 13, 25 , 26 and 30 depend) and claim 23 (upon which claim 24 depends) in accordance with the Examiner's suggestion for expediting prosecution only. The amendment to claim 12 recites the limitation that the subject DNA is useful in securing expression of a polypeptide, ". . . *wherein said primary structural conformation comprises as a mature protein an amino acid sequence at its amino terminal end at least the amino acid residues 1 to 42 of Figure 2, . . .* " Amendment to claim 23 adds the limitation, " . . . *wherein said polypeptide fragment or polypeptide analog has at its N-terminus at least amino acid residues 1 to 42 of Figure 2., and (b) one or more of the biological properties of naturally-occurring metalloproteinase inhibitor. . .* " It is believed that the above amendments place the claims in condition for allowance. Entry and consideration of the amendment is respectfully requested.

Objection to the Specification and Rejection of Claims 23 Pursuant to 35 USC § 112.

As noted above, to expedite prosecution, Applicant's have amended claim 23. But, regardless, the analogs and fragments recited are adequately disclosed in the specification. For example, at page 10, line 33 through page 11, line 28, MI products such as polypeptide analogs of MI and fragments of MI are described, and procedures for preparation of their DNA's are noted (e.g., Alton et al., WO 83/04053). Further, means for testing for biological activity are plainly disclosed (e.g., Example 11 at page 64 et seq.)

One is therefore instructed on "how to make" the recited DNA. Applicants submit that this is a matter of trial and error. In re Wands , discussing monoclonal antibody art, is instructive on this point. 8 USPQ2d 1400

(Fed. Cir. 1988). In Wands, generic claims to antibodies against hepatitis were found to be enabled despite the screening process which may have been laborious for the ordinary skilled artisan:

> The nature of monoclonal antibody technology is that it involves screening hybridomas to determine which ones secrete antibody with desired characteristics. Practitioners of this art are prepared to screen negative hybridomas in order to find one that makes the desired antibody. No evidence was presented by either party on how many hybridomas would be viewed by those in the art as requiring undue experimentation to screen. However, it seems unlikely that undue experimentation would be defined in terms of the number of hybridomas that were never screened. Furthermore, in the monoclonal antibody art it appears that an 'experiment' is not simply the screening of a single hybridoma, but is rather the entire attempt to make a monoclonal antibody against a particular antigen. This process entails immunizing animals, fusing lymphocytes from the immunized animals with myeloma cells to make hybridomas, cloning the hybridomas, and screening the antibodies produced by the hybridomas for the desired characteristics. Wands carried out this entire procedure three times, and was successful each time in making at least one antibody that satisfied all of the claimed limitations. Reasonably interpreted, Wands' record indicates that, in the production of high-affinity IgM antibodies against HBsAG, the amount of effort-□ needed to obtain such antibodies is not excessive. Wand's evidence thus effectively rebuts the examiner's challenge to the enablement of their disclosure. [Footnote omitted]

Presently, the end product is disclosed (either in the amended or in the unamended claim; viz.: the subject DNA), the means to make such DNA are disclosed (e.g., site-directed mutagenesis), and the ways to recognize the end-product~~is~~are disclosed (e.g., the in vitro assays of Example 11). Using trial-and-error, a practitioner would have been enabled at the time of filing to obtain the claimed DNAs.

The Examiner has pointed to nothing to call the above-referenced passages into question. In re Marzocchi, 169 USPQ 367, 370 (CCPA 1971) (Reversing Board decision that a claim broadly reciting the use of amine compounds was not enabled, stating inter alia, "[I]t is incumbent upon the Patent Office, whenever a rejection on this [lack of enablement] basis is made,

to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." )

Applicants note that (unamended) claims 23 and 24 were rejected as being obvious over references directed to bovine-originating material. The obviousness rejection indicates that the Examiner's position is that the claimed subject matter would have been within the skill of the art at the time the invention was made. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 231 USPQ 81 (Fed. Cir. 1986) cert. denied, 480 U.S. 947 (1987). The view that the recited DNA was within the skill of the art at the time of filing is inconsistent with the position that the recited DNA is not enabled.

For the above reasons, Applicants respectfully request consideration of this paper and entry of the above amendments. It is submitted that the claims are now in condition for allowance.

The Commissioner is authorized to charge any fees associated with this application to Deposit Account Number 01-0519. Any questions associate with this application may be directed to Applicants' attorney at 805/447-2193.

Respectfully submitted,

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By: Karol Pessin

Karol Pessin
Registration No. 34, 899

Amgen Inc.
1840 Dehavilland Drive
Thousand Oaks, CA 91320
805/447-2193